

Translation

PATENT COOPERATION TREATY

PCT/JP2003/016523



PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY (Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference POKJ-10390	FOR FURTHER ACTION See Form PCT/IPEA/416	
International application No. PCT/JP2003/016523	International filing date (day/month/year) 24 December 2003 (24.12.2003)	Priority date (day/month/year) 24 December 2002 (24.12.2002)
International Patent Classification (IPC) or national classification and IPC C12P 19/28, C08B 37/00		
Applicant KAJIHARA, Yasuhiro		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 7 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
 - a. ☒ (sent to the applicant and to the International Bureau) a total of 7 sheets, as follows:
 - ☒ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
 - ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
 - b. ☒ (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) disk, 1, containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

- | | |
|--|---|
| <input checked="" type="checkbox"/> Box No. I | Basis of the report |
| <input type="checkbox"/> Box No. II | Priority |
| <input type="checkbox"/> Box No. III | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability |
| <input checked="" type="checkbox"/> Box No. IV | Lack of unity of invention |
| <input checked="" type="checkbox"/> Box No. V | Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement |
| <input checked="" type="checkbox"/> Box No. VI | Certain documents cited |
| <input type="checkbox"/> Box No. VII | Certain defects in the international application |
| <input type="checkbox"/> Box No. VIII | Certain observations on the international application |

Date of submission of the demand 11 June 2004 (11.06.2004)	Date of completion of this report 01 December 2004 (01.12.2004)
Name and mailing address of the IPEA/JP	Authorized officer
Facsimile No.	Telephone No.

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Box No. I Basis of the report

1. With regard to the language, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

- ☐ This report is based on translations from the original language into the following language _____, which is language of a translation furnished for the purpose of:
- ☐ international search (under Rules 12.3 and 23.1(b))
 - ☐ publication of the international application (under Rule 12.4)
 - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the elements of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

- ☐ The international application as originally filed/furnished
- ☒ the description:
- pages _____ 1-93 _____, as originally filed/furnished
- pages* _____ received by this Authority on _____
- pages* _____ received by this Authority on _____
- ☒ the claims:
- pages _____ 2-6, 9-11, 14-20 _____, as originally filed/furnished
- pages* _____, as amended (together with any statement) under Article 19
- pages* 1, 7, 8, 12, 13, 21, 22, 24-28 received by this Authority on 15 November 2004 (15.11.2004)
- pages* _____ received by this Authority on _____
- ☐ the drawings:
- pages _____, as originally filed/furnished
- pages* _____ received by this Authority on _____
- pages* _____ received by this Authority on _____
- ☒ a sequence listing and/or any related table(s) – see Supplemental Box Relating to Sequence Listing.

3. ☒ The amendments have resulted in the cancellation of:

- ☐ the description, pages _____
- ☒ the claims, Nos. _____ 23 _____
- ☐ the drawings, sheets/figs _____
- ☐ the sequence listing (*specify*): _____
- ☐ any table(s) related to sequence listing (*specify*): _____

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

- ☐ the description, pages _____
- ☐ the claims, Nos. _____
- ☐ the drawings, sheets/figs _____
- ☐ the sequence listing (*specify*): _____
- ☐ any table(s) related to sequence listing (*specify*): _____

* If item 4 applies, some or all of those sheets may be marked "superseded."

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Box No. IV Lack of unity of invention

1. ☐ In response to the invitation to restrict or pay additional fees the applicant has:
 - ☐ restricted the claims.
 - ☒ paid additional fees.
 - ☐ paid additional fees under protest.
 - ☐ neither restricted nor paid additional fees.
2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.
3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is
 - ☒ complied with.
 - ☐ not complied with for the following reasons:

In accordance with the correction made by Amendment on November 15, 2004, the matters shared by the inventions of claims 1-22 and 24-28 include "a fluorine-containing sugar chain asparagine in which the one amino group nitrogen of the asparagine has been protected by a lipid-soluble protective group. Because the above item is novel, the inventions of claims 1-22 and 24-28 satisfy the requirement for unity of invention.

4. Consequently, this report has been established in respect of the following parts of the international application:
 - ☒ all parts.
 - ☐ the parts relating to claims Nos. _____

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Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)

Claims

1-22, 24-28

YES

Claims

NO

Inventive step (IS)

Claims

YES

Claims

1-22, 24-28

NO

Industrial applicability (IA)

Claims

1-22, 24-28

YES

Claims

NO

2. Citations and explanations (Rule 70.7)

Document 1:

Haneda K. et al. Transglycosylation of intact sialo complex-type oligosaccharides to the *N*-acetylglucosamine moieties of glycopeptides by *Mucor hiemalis* endo- β -*N*-acetylglucosaminidase, Carbohydrate Research, October, 1996, Vol. 292, pages 61-70

Document 2:

Unverzagt C., Building blocks for glycoproteins: Synthesis of the ribonuclease B fragment 21-25 containing an Undecasaccharide N-glycan, Tetrahedron Letters, August, 1997, Vol. 38, No. 32, pages 5627-5630

Document 3:

Unverzagt C. Chemoenzymatic synthesis of a sialylated diantennary N-glycan linked to asparagine, Carbohydrate Research, December, 1997, Vol. 305, pages 423-431

Document 4:

Yasuhiro Kajiwarra et al., "Asparagine ni Ketsugo shita 2bunki Fukugogata Tosa Yudotai no Gosei to NMR ni yoru Kozo Kaiseki," Dai 22 Kai The Japanese Society of Carbohydrate Research Nenkai Yoshishu, 02 July, 2001, page 33

Document 5:

Lin CH, et al., Enzymatic synthesis of a sialyl Lewis X dimer from egg yolk as an inhibitor of E-selectin., Bioorganic and Medicinal Chemistry, December, 1995, Vol. 3, no. 12, pages 1625-1630

Document 6:

Inazu T. et al., Preparation of Fmoc-asparagine derivatives having natural *N*-linked oligosaccharide, and its application to the synthesis of glycopeptides, Peptide Science, 1999, Vol. 1998, pages 153-156

Document 7:

JP, 2000-169503, A (Seikagaku Corp.), 20 June, 2000, pages 24-32

Document 8:

US, 5908766, A (Japan Tobacco Inc.), 01 June, 1999

Document 9:

JP, 08-9989, A (Meiji Milk Products CO., Ltd.), 16, January, 1996

Document 10:

JP, 2002-45196, A (Toyobo Co., Ltd.), 12 February, 2002 (Family: none)

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Box No. VI Certain documents cited

1. Certain published documents (Rule 70.10)

Application No. Patent No.	Publication date (day/month/year)	Filing date (day/month/year)	Priority date (valid claim) (day/month/year)
WO 03/008431 A1 [EX]	30.01.2003	19.06.2002	19.06.2001

2. Non-written disclosures (Rule 70.9)

Kind of non-written disclosure	Date of non-written disclosure (day/month/year)	Date of written disclosure referring to non-written disclosure (day/month/year)

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Supplemental Box Relating to Sequence Listing

Continuation of Box No. 1, item 2:

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this report was established on the basis that of:
 - a. type of material
 - ☒ a sequence listing
 - ☐ table(s) related to the sequence listing
 - b. format of material
 - ☐ in written format
 - ☒ in computer readable form
 - c. time of filing/furnishing
 - ☐ contained in the international application as filed
 - ☒ filed together with the international application in computer readable form
 - ☐ furnished subsequently to this Authority for the purpose of search and/or examination
 - ☐ received by this Authority as an amendment* on _____
2. ☒ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
3. Additional comments:

** If item 4 in Box No. 1 applies, the listing and/or table(s) related thereto, which form part of the basis of the report, may be marked "superseded".*

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.
Continuation of Box V:

Document 11: Edited by The Japanese Biochemical Society, "Shin Seikagaku Jikken Koza (Dai 3 Kan), Toshitsu I To-Tanpakushitsu (Jo)," Tokyo Kagaku Dojin, May 21, 1990, pages. 312-349.

Based on the descriptions in documents 1-11, the inventions of claims 1-22, and 24-28 lack an inventive step.

Documents 1-5 describe sugar chain asparagines that contain and do not contain Fmoc.

Documents 1 and 6 describe refining the sugar chain asparagine derivative containing Fmoc using chromatography. This examination finds that applying the same to the inventions of documents 1-5 does not present any particular technical difficulty.

In addition, a means for introducing fluorine to a sugar chain such as sialic acid, and the fact that sialic acid containing a fluorine has physiological activity such as inhibition of sialidase were widely known prior to the filing date of this application (if necessary see document 7, WO 95/32955 A, WO 98/11083 A, JP 1-287029 A, etc.) Therefore, this examination finds that persons skilled in the art can easily conceive of introducing fluorine at the sialic acid site in the sugar chain asparagines of the inventions described in documents 1-5.

In addition, documents 8-11 describe the hydrolysis of sugar chains and the production of various sugar chains by an exoglycosidase such as sialyl transferase, galactose hydrolase, mannose hydrolase, or N-acetylglucosamine hydrolase, etc. In addition, document 5 describes the transfer of fucose to the N-acetylglucosamine of a sugar chain asparagine.

In a written reply the applicant asserts that resistance to sialidase is increased and the sugar chain derivative is not broken down as a result of the addition of fluorine to the sugar chain, but because it was widely known before the priority date of this application that sialic acid containing fluorine has sialidase inhibitory activity, this examination finds that the effect provided thereby is not so outstanding that it could not be predicted by persons skilled in the art.